
Neural Precursor-Derived Pleiotrophin Mediates Subventricular Zone Invasion by Glioma.

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Public Summary:

The lateral ventricle subventricular zone (SVZ) is a frequent and consequential site of pediatric and adult glioma spread, but the cellular and molecular mechanisms mediating this are poorly understood. We demonstrate that neural precursor cell (NPC):glioma cell communication underpins this propensity of glioma to colonize the SVZ through secretion of chemoattractant signals toward which glioma cells home. Biochemical, proteomic, and functional analyses of SVZ NPC-secreted factors revealed the neurite outgrowth-promoting factor pleiotrophin, along with required binding partners SPARC/SPARCL1 and HSP90B, as key mediators of this chemoattractant effect. Pleiotrophin expression is strongly enriched in the SVZ, and pleiotrophin knock down starkly reduced glioma invasion of the SVZ in the murine brain. Pleiotrophin, in complex with the binding partners, activated glioma Rho/ROCK signaling, and ROCK inhibition decreased invasion toward SVZ NPC-secreted factors. These findings demonstrate a pathogenic role for NPC:glioma interactions and potential therapeutic targets to limit glioma invasion.

Scientific Abstract:

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